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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/011,940	03/03/99	NAUCK M	564861USWO

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EXAMINER	
CELSA, B	

ART UNIT	PAPER NUMBER
1627	21

DATE MAILED: 08/30/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

file copy

Office Action Summary

Application No.	Applicant(s)
09/011,940	Nauck et al.
Examiner	**Art Unit**
Bennett Celsa	1627

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 20, 2001*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 17-26, 28-39, and 41-50* is/are pending in the application.

4a) Of the above, claim(s) *26, 28-31, and 36-39* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 17-25, 32-35, and 41-50* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Response to Amendment

Applicant's amendment dated 6/20/01 in paper no. 20 is hereby acknowledged.

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of the Claims

Claims 1-2, 17-26 and 28-39 and 41-50 are currently pending.

Claims 26, 28-31 and 36-39 are withdrawn from consideration as being directed to a nonelected invention.

Claims 1-2, 17-25, 32-35 and 41-50 are currently under consideration.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Withdrawn Objection (s) and/or Rejection (s)

Applicant's amendment has overcome the following rejections of claims 41 and 44:

a. Under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention (Lack of Written Description)

b. Under 35 U.S.C. 112, first paragraph, as based on a disclosure which:

a. Lacks essential subject matter (e.g. See *Ex parte Bhide* cited below); AND

b. Is not enabling for both making and use.

c. Under 35 U.S.C. 112, first paragraph for new matter (item B. in the prior office action).

d. Under 35 U.S.C. 112, second paragraph for indefiniteness.

Applicant's argument has overcome the new matter rejection of claim 20 for the term "nutrient".

Applicant's arguments have overcome the rejection of claims 1-2, 17-18, 21-25, 32-33, 35 and 41, 44, 45, 47 under 35 U.S.C. 102(b) as being anticipated by Habener, U.S. Pat. No. 5,118,666 (6/92).

Outstanding Objection (s) and/or Rejection (s)

Claim Rejections - 35 USC § 112

3. Claim 21 (and claims dependent thereon) are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

A. The new limitation of claim 21, e.g. "are administered at a rate of 0.01 ... per minute" constitutes new matter to extent that these recited amounts encompass parenteral administration means other than "infusion". In other words, the specification only provides support for this limitation with respect to administration by infusion.

Discussion

Applicant's amendment and arguments directed to the above new matter rejection were considered but deemed nonpersuasive for the following reasons.

Applicant's arguments directed to item A. (Rejection of claim 21) above was considered but deemed nonpersuasive for the following reasons.

Applicant argues that "administration" was originally present in the claim and "infusion" represents only one specific type of "administration" which is supported by the specification.

Applicant's argument fails to address the rejection which is directed to the fact that the specification only teaches "Suitable infusion rates" which include "0.01-50 picomole" (see specification page 9, bottom). Amending to extend infusion rates to any other means of parenteral administration constitutes new matter.

Accordingly, this rejection is hereby maintained

4. Claims 20, 41 and 44 (and claims dependent thereon) are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 20, "the source of carbohydrate nutrients" lacks clear antecedent basis.

Discussion

Applicant's arguments directed to the above indefinite rejection were considered but deemed nonpersuasive for the following reasons.

Applicant reproduces amended claim 20 and then argues that the term "the source of carbohydrate nutrients" has been deleted (e.g. from the preamble of the claim) thus obviating this rejection.

However, lines 4-5 of amended claim 20 still contains the phrase "the source of carbohydrate nutrients" to which there is no antecedent basis.

Accordingly, this rejection is hereby maintained.

5. Claims 1-2, 17-19, 21-25, 32-35 and 41-48 are rejected under 35 U.S.C. 102(e) as being anticipated by Habener) as being anticipated by Habener, U.S. Pat. No 5,614,492 (3/97: filed 9/91 or earlier).

Habener "492 disclose the use of GLP 1 and its derivatives (e.g. col. 7) to treat both diabetes and hyperglycemia (e.g. see col. 6, lines 1-10) due to the peptide's "insulinotropic" activity (e.g. see col. 5, line 60-70). "Parenteral administration" of GLP 1 and its derivatives in pharmaceutical compositions comprising carbohydrates (e.g. lactose), polyamino acids: controlled release formulations comprising lipid derivatives (e.g. liposomes) e.g. see bottom of col. 9 to top of col. 10) as well as conjugates thereof (e.g. see col. 10, lines 13-26) anticipate the presently claimed invention. Further Example 11 (e.g. col. 21-28, especially "meal studies") disclose the

administration of GLP-1 both during a meal (e..g 50% CHO; 30% fat; 20% protein: see e.g. col. 22, lines 55-67) and postprandial to both NORMAL and non-diabetic patients with the successful control of plasma glucose levels. See also patent claims 1 and 9 (and dependent claims thereon) teaching the use of GLP-1 and derivatives to treat diabetes and hyperglycemia.

Accordingly, the parenteral administration of GLP-1 and its derivatives before/during/after meals that both contained and generated CHO (e.g. especially glucose) anticipates the presently claimed invention. See also patent claims which additionally disclose the treatment of both diabetes and hyperglycemia utilizing GLP-1 containing compositions.

Discussion

Applicant's arguments directed to the above anticipation rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that the Habener reference at column 9 teaches parenteral administration of an insulinotropic agent which is "not administered in the presence of a nutritively effective amount of a nutrient"

However, as recited in the rejection above, the Habener reference clearly teaches the "preferred" (e.g. see col. 9, lines 1-4) administration of GLP-1 (and derivatives) in combination with (both in separate or combined form e.g. conjugated and unconjugated) pharmaceutically acceptable carriers and delivery agents, which include compounds clearly within the scope of the term "nutrient" (e.g. lactose, polyamino acids: **see col. 9-10**). Applicant's arguments directed to the "nutritively effective amounts" are not commensurate in scope to the presently claimed

invention which are not limited to a "nutritively effective amount"; nor has applicant provided any evidence whatsoever that the reference amounts would not obtain nutrition within the scope of the presently claimed invention. .

Accordingly, the above rejection is hereby maintained.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 17-25, 32-35 and 41-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Specification disclosure as to the state of the prior art in view of Habener, U.S. Pat. No. 5,614,492 (3/97: filed 9/91 or earlier) and/or Eng US Pat. No. 5,424,286 (6/95) .

The specification on pages 1-2 and page 10, lines 15 describes the state of the prior art regarding the necessity for providing parenteral nutrition to patients having "disturbed glucose metabolism" (e.g. surgery patients, shock etc) as well as to malnourished patients while overcoming the hyperglycemia that accompanies parenteral nutrition. Coadministration of insulin with parenteral nutrition in order to overcome the hyperglycemia problem has its drawbacks (e.g. see page 1, lines 13-25).

The State of the Prior Art as described in the specification differs from the presently claimed invention which incorporates the use of "insulinotropic peptides" (e.g. GLP-1 and its derivatives) in parenteral nutrition compositions which comprise nutrients (e.g. glucose or glucose generating compounds) for alimentary nutrition or to treat hyperglycemic states.

However, both the Habener and Eng Patent references teach the "insulinotropic" nature of GLP-1 and related peptides e.g. the ability of these peptides to endogenously generate insulin and thus combat hyperglycemia.

Additionally, the prior/sequential and co-administration of these "insulinotropic" peptides with a meal containing nutrients (e.g. which include glucose or generate glucose) and the peptides concomitant ability to obtain normalized glucose levels is both disclosed and suggested by the Habener and/or Eng patents (e.g. see Habener, Example 11, col. 21-28 and patent claims

addressing treatment of diabetes and hyperglycemia; e.g. see Eng at col. 1, lines 49-67 disclosing lowering of meal-related glucose levels by parenteral administration of GLP-1 and GLIP which effect was also found with other "insulinotropic" peptides (e.g. exendins) alone or in combination (including sequential) with GLP-1 (e.g. see Eng col. 2, lines 35-40; col. 5, lines 14-20; Example 2 (col. 6-7); Example 5 relating to diabetics; and patent claims 5-6.

The determination of optimal amounts of "insulinotropic" peptides and/or nutrients taken sequentially or in combination is well within the skill of the art as well as the determination of optimal delivery formulations (e.g. tablets, pills, delayed release etc.) and time of delivery (e.g. coadministered, sequential etc.).

One of ordinary skill in the art would be motivated to substitute the "insulinotropic" peptides disclosed by the Eng or Habener references for insulin in "parenteral" formulations as disclosed in the Specification, due to the problematic use of insulin as discussed in the specification and in view of the ability of "insulinotropic peptides" to endogenously produce insulin as taught by the Eng and/or Habener references.

Accordingly, the incorporation of "insulinotropic" peptides (e.g. GLP-1 or its derivatives) into parenteral formulations containing "nutrients" to treat diabetics, non-diabetics (e.g. hyperglycemia) or malnourished individuals would have been obvious to one of ordinary skill in the art at the time of applicant's invention in view of the Habener and/or Eng references which demonstrate that administration of these peptides to obtain normalized glucose levels; regardless of the cause of hyperglycemia (meal/diabetes/hyperglycemia etc.).

Discussion

Applicant's arguments directed to the above obviousness rejection were considered but deemed nonpersuasive for the following reasons.

Applicant argues that Eng teaches administration of insulinotropic compounds attached to carrier molecules that are not delivered in nutritively effective amounts; and that Eng teaches removal of "nutrients" from the insulinotropic compositions. . This argument is not found convincing for the following reasons.

In response to applicant's arguments against the Eng reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Secondly, applicant has not pointed out where Eng teaches the removal of "nutrients".

Thirdly, applicant has failed to rebut the teaching of the Eng Patent reference recited in the above rejection e.g. that Eng teaches the "insulinotropic" nature of GLP-1 and related peptides e.g. the ability of these peptides to endogenously generate insulin and thus combat hyperglycemia and normalize glucose levels..

Applicant next argues that the '492 patent "teaches away" from including "nutrients" referring to the portion (e.g. col. 9, lines 21-26) of the '492 patent which refers to peptides and carbohydrates as "contaminants". This argument is not found persuasive for the following reasons. In response to applicant's arguments against the '492 patent reference individually,

one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Secondly, applicant has failed to consider the '492 reference teaching as a whole which specifically teaches the "preferred" (e.g. see col. 9, lines 1-4; col. 9-10) incorporation of "carriers" and dosage forms which contain compounds which constitute "nutrients" within the scope of the presently claimed invention.

Thirdly, applicant has failed to rebut the teaching of the '492 patent reference recited in the above rejection e.g. that the '492 patent teaches the "insulinotropic" nature of GLP-1 and related peptides e.g. the ability of these peptides to endogenously generate insulin and thus combat hyperglycemia and normalize glucose levels..

Applicant next argues that the specification teaches that "Traditional nutritional therapies use a low rate of parenteral nutrient administration so that blood sugar level does not exceed normal physiological limits " and that the advantage of the present invention is that "requisite nutrients may be delivered parenterally while maintaining an appropriate blood sugar level".

However, applicant fails to address the specification admission as to the nature of the prior art as described in the rejection above. As pointed out in the rejection above, the specification on pages 1-2 and page 10, lines 15 describes the state of the prior art regarding the necessity for providing parenteral nutrition to patients having "disturbed glucose metabolism" (e.g. surgery

patients, shock etc) as well as to malnourished patients while overcoming the hyperglycemia that accompanies parenteral nutrition. Coadministration of insulin with parenteral nutrition in order to overcome the hyperglycemia problem has its drawbacks (e.g. see page 1, lines 13-25).

The issue addressed in the above obviousness rejection is simply whether it would have been obvious to substitute insulinotropic peptides (E.g. peptides which stimulate insulin release) for insulin in conventional compositions of insulin and nutrients administered to patients in need thereof.

As pointed out in the obviousness rejection above, the prior art (Habener and/or Eng) recognize that concomitant administration of "insulinotropic" peptides with a meal containing nutrients (e.g. which include glucose or generate glucose) would obtain *normalized glucose* levels which renders the solution to the problem present in the prior art insulin and nutrient compositions obvious e.g. substitute an "insulinotropic" peptide for insulin to avoid the "insulin" problem of causing hyperglycemia which is acknowledged by the specification as being known in the prior art

Applicant has failed to address why it would not be obvious to replace problematic insulin with an insulinotropic peptide in the disclosed prior art parenteral nutrition formulations in light of the motivation to do so provided by both the Habener and Eng references and as discussed in the obviousness rejection above.

Accordingly, the above obviousness rejection is hereby maintained.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

General information regarding further correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Celsa whose telephone number is (703) 305-7556.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat (art unit 1627), can be reached at (703)308-0570.

Any inquiry of a general nature, or relating to the status of this application, should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Bennett Celsa (art unit 1627)

August 28, 2001

BENNETT CELSA
PRIMARY EXAMINER